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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,014	12/12/2003	Audrey Goddard	10466/486	2599

7590 02/22/2006

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CHICAGO, IL 60610

EXAMINER

KAUSHAL, SUMESH

ART UNIT	PAPER NUMBER
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1633

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

10/735,014

Applicant(s)

GODDARD ET AL.

Examiner

Sumesh Kaushal Ph.D.

Art Unit

1633

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 30 December 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.  
b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

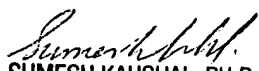
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: \_\_\_\_\_.  
Claim(s) withdrawn from consideration: \_\_\_\_\_.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

  
SUMESH KAUSHAL, PH.D.  
PRIMARY EXAMINER

Sumesh Kaushal  
Primary Examiner  
Art Unit: 1633

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Continuation of 11. does NOT place the application in condition for allowance because: Claims 22-26 stand rejected under 35 USC 101 regarding Utility issues and under 35 USC 112(1) regarding Enablement issues for the same reasons of record as set forth in the office action mailed on 11/1/05. The invention as claimed lacks Utility and is found not enabled because instant specification (as filed) does not teach any significance or functional characteristics of the PRO0361 polypeptide (SEQ ID NO:83) or antibody. The specification does not even disclose if PRO0361 is a secreted protein or a transmembrane protein. However, applicant argues that example 34, found on page 141 discloses that the PRO361 polypeptide tested positive in the Mixed Lymphocyte Reaction (MLR) Assay. The applicant asserts that a positive reaction in the MLR assay illustrates that PRO361 functions as an inhibitor of the proliferation of stimulated T-lymphocytes. However, applicant's arguments are found not persuasive. The earlier office action clearly states that the ability of a protein to stimulate lymphocyte proliferation in the MLR assay does not support a specific and substantial utility for the claimed invention. The ability to stimulate or inhibit lymphocyte proliferation in the MLR assay is an artificial in-vitro system and does not provide for what specific conditions or for which specific diseases the claimed invention would predictably function. The assertion that the claimed invention could be useful for the treatment of conditions where the enhancement of the immune response would be beneficial is not specific, since there are many such conditions, and it is not predictable of which conditions the claimed invention may function, if any. Mixed lymphocyte culture (MLC or MLR) is a special case of antigen stimulation in which T lymphocytes respond to foreign histocompatibility antigen on unrelated lymphocytes or monocytes. MLC is a functional assay of cellular response to stimulatory determinants associated predominantly with HLA class II molecules. A single genetic locus or region, known as HLA, controls the MLC reactivity. The MLC assay recognizes disparate HLA class II molecules and the resulting T-cell activation, which is thought to represent an in vitro model of the afferent arm of the in vivo allograft reaction. The degree of reactivity observed correlates with the degree of antigenic disparity between responding and stimulating cells. Briefly, when the lymphocytes of 2 HLA-disparate individuals are combined in tissue culture, the cells enlarge, synthesize DNA, and proliferate, whereas HLA-identical cells remain quiescent. Since both cells will normally proliferate, a one-way test is used to monitor the response of a single responder cell by inactivating the stimulator cell by radiation or drugs in order to inhibit DNA synthesis of the stimulator cell. The proliferation is driven primarily by the differences in the class II HLA antigens between the 2 test cells (or individuals). This reaction is not predictive of general responses of the immune system because, in vivo, activation of a lymphocyte is controlled not only by antigen binding but also by interactions with other cells. All T cells must cooperate with antigen-presenting cells, whereas B cells and cytotoxic T cells depend on helper T lymphocytes. These interactions either require direct surface-to-surface contact or are mediated by cytokines that act only over extremely short distances. Because of this interdependence, lymphocyte activation occurs commonly and efficiently in the secondary lymphoid organs, where lymphocytes, antigens, and antigen-presenting cells encounter one another at close quarters. Therefore, the MLC assay, which is art recognized for determining histocompatibility, does not appear to be predictive of general immune responses in vivo. The specification indicates that CD4-IgG was used as a control, but it is not clear how this would control for background stimulation or provide for a measure of maximal stimulation. Lastly, the specification fails to provide any data or evidence of the results of the assay, therefore, one of ordinary skill in the art cannot evaluate the conclusion. The specification states that "positive increases over control are considered positive", however, this does not indicate that statistical significance must occur for determination of a positive result in the assay. Even though the applicant argues that the PRO polypeptide inhibits the lymphocyte proliferation like an IL-12 molecule via dendritic cell interaction the specification fails to provide. Even though the applicant argues that the MLR assay of the present application is designed to measure the ability of a test substance to "drive" the dendritic cells to induce the proliferation of T-cells that are activated or co-stimulated in the MLR assay like an IL-12 molecule the specification fails to provide any evidence that PRO polypeptide as claimed is capable of driving the dendritic cells to induce the proliferation of T-cells in the MLR assay via well establishes and specific interaction. In conclusion, the results of the MLR assay do not support a specific and substantial utility for the claimed invention because the assay is not predictive of immune response in general, and one of ordinary skill in the art would not expect a stimulatory effect in the MLC assay to correlate to a general stimulatory effect on the immune system, absent evidence to the contrary. Thus the only immediate apparent utility for the instant invention would be further scientific characterization of PRO361 polypeptide and an antibody that binds to this protein. Therefore, the asserted utility is not substantial, as the real-world use has not been established. Thus, the proposed use of the claimed antibodies that bind PRO361 polypeptides are simply starting points for further research and investigation into potential uses of the polypeptides. See *Brenner v. Manon*, 148 U.S.P.Q. 689 (Sup. Ct. 1966), wherein the court held that: The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility; "[u]nless and until a process is refined and developed to this point- where specific benefit exists in currently available form- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[I]t is not a reward for the search, but compensation for its successful conclusion." The only immediate apparent utility for the instant invention would be further scientific characterization of PRO361 polypeptide and an antibody that binds to this protein.

In addition the instant specification does not comply with 35 U.S.C. 101 and 112 since nebulous expressions "biological activity" and "biological properties" do not contain a sufficiently explicit indication of usefulness of compounds and how to use them. The utility requirements must be met at the time of filing and not after someone else identifies a utility that had not been disclosed in the specification. The disclosure is insufficient where experimentation is necessary to determine actual uses, or possible lack of uses, of compounds, as well as how to employ them in a useful manner. For example, it cannot be presumed that a steroid chemical compound is "useful" under 35 U.S.C. 101, or that one skilled in the art will know "how to use" it, simply because compound is closely related only in a structural sense to other steroid compounds known to be useful (In re Kirk and Petrow, 153 USPQ 48 (CCPA 1967)). In instant case the mere presence of mucin protein-like structure does not teach one skill in the art how to use the invention as claimed, since the disclosure is insufficient and requires further experimentation necessary to determine actual uses or possible lack of uses of the polypeptide, as well as how to employ them in a useful manner. It cannot be presumed that an antibody to PRO361 polypeptide is useful under 35 USC 101/112 or that one skilled in the art will know "how to use" it, simply because polypeptide is closely related only in a structural sense to other mucin-like proteins known to be useful. Therefore, the asserted use for the claimed invention is not supported by either a specific and/or substantial utility, since no function can be ascribed to the gene product. The only immediate apparent utility for the instant invention would be further scientific characterization of PRO361 polypeptide and an antibody that binds to this protein.